

IN THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

Claims 1-2 (canceled).

Claim 3 (previously presented): A method for isotopically labeling a functional group possessed by an amino acid residue of a protein, comprising the step of reacting a transglutaminase with said protein in the presence of an isotope-labeled ammonium salt.

Claim 4 (previously presented): The method of Claim 3, wherein said amino acid residue is a glutamine residue and said functional group is a  $\gamma$ -carboxamido group.

Claim 5 (previously presented): The method of Claim 3, wherein said transglutaminase is calcium-independent.

Claim 6 (previously presented): The method of Claim 3, wherein said transglutaminase is calcium-dependent and said reacting said transglutaminase with said protein is conducted in the presence of calcium.

Claim 7 (previously presented): The method of Claim 3, wherein said transglutaminase is reacted with said protein in an aqueous environment at a pH of about pH5.0 to pH9.0 and a temperature of 4°C to 55°C for a time of about 30 seconds to about 2 days.

Claim 8 (previously presented): The method of Claim 3, wherein the ratio of the concentration of said ammonium salt to the concentration of said protein to be labeled is more than about 10.

Claim 9 (previously presented): The method of Claim 8, wherein the concentration of said protein to be labeled is about 1 $\mu$ M to about 40mM and the concentration of said ammonium salt is about 10 $\mu$ M to about 10M.

Claims 10-15 (canceled).

Claim 16 (currently amended): An isotopically labeled protein, prepared by a process, comprising reacting a transglutaminase with a protein in the presence of an isotope-labeled ammonium salt, wherein said protein contains at least one glutamate glutamine residue on which said transglutaminase does not act and at least one glutamate glutamine residue on which said transglutaminase does act.

Claim 17 (previously presented): The isotopically labeled protein of Claim 16, wherein said transglutaminase is reacted with a functional group of an amino acid residue and said amino acid residue is a glutamine residue and said functional group is a  $\gamma$ -carboxamido group.

Claim 18 (previously presented): The isotopically labeled protein of Claim 16, wherein said transglutaminase is calcium-independent.

Claim 19 (previously presented): The isotopically labeled protein of Claim 16, wherein said transglutaminase is calcium-dependent and said reacting said transglutaminase with said protein is conducted in the presence of calcium.

Claim 20 (previously presented): The isotopically labeled protein of Claim 16, wherein said transglutaminase is reacted with said protein in an aqueous environment at a pH of about pH5.0 to pH9.0 and a temperature of 4°C to 55°C for a time of about 30 seconds to about 2 days.

Claim 21 (previously presented): The isotopically labeled protein of Claim 16, wherein the ratio of the concentration of said ammonium salt to the concentration of said protein to be labeled is more than about 10.

Claim 22 (previously presented): The isotopically labeled protein of Claim 21, wherein the concentration of said protein to be labeled is about 1 $\mu$ M to about 40mM and the concentration of said ammonium salt is about 10 $\mu$ M to about 10M.

Claim 23 (currently amended): The isotopically labeled protein of Claim 16, wherein said glutamate glutamine residue on which said transglutaminase acts is introduced into the protein by site-directed mutagenesis.

Claim 24 (previously presented): The isotopically labeled protein of Claim 16, wherein said transglutaminase acts under a condition in which the three-dimensional structure of said protein is retained.

SUPPORT FOR THE AMENDMENTS

Applicants have amended Claims 16 and 23 to replace the term “glutamate” with “glutamine” and page 5, lines 8 and 9 to replace “glutamic acid” with “glutamine”.

Applicants submit that the amendment serves to correct an obvious error in the relevant sections above. Moreover, Applicants submit that the correction would be obvious to the skilled artisan for the following reasons.

The specification describes, at length, that a transglutaminase catalyzes the acyl transfer reaction of the  $\gamma$ -carboxyamide of the glutamine residue present in the peptide chain of a protein molecule (see, for example, page 7, lines 4-6). Applicants note that the artisan would readily appreciate that a glutamate residue does not have a  $-NH_2$  group that can be labeled and that a glutamic acid residue does not have a carboxyamide nitrogen.

Further, throughout the specification (for example at page 8, lines 13-16, page 10, lines 11-13, page 13, lines 7-11, and page 23, lines 17-18) the correct term “glutamine residue” is used rather than the improper “glutamic acid residue” or “glutamate residue.” Moreover, the labeled residue would also be apparent from the description provided in the Examples. Additional support for the amended claims themselves can be obtained by reference to page 10, lines 21-24, as well.

For these reasons, the amendment to Claims 16 and 23 to replace the term “glutamate” with “glutamine” and page 5, lines 8 and 9 to replace “glutamic acid” with “glutamine” does not constitute new matter.